TUBB3 gene

tubulin beta 3 class III

Normal Function

The *TUBB3* gene provides instructions for making one version of a protein called beta-tubulin (β-tubulin). This protein is part of the tubulin family of proteins that form and organize cell structures called microtubules. Microtubules are rigid, hollow fibers that make up the cell's structural framework (the cytoskeleton). They are composed of β-tubulin and a similar protein called alpha-tubulin (α-tubulin) that is produced from a different gene. Microtubules grow and shrink as tubulin proteins are added to and removed from the ends of fibers. This process allows cells to move and change shape.

β-tubulin produced from the *TUBB3* gene is found in nerve cells (neurons) in the brain. This β-tubulin protein plays a role in the growth of specialized nerve cell extensions called axons and dendrites (collectively called neurites). Studies show this protein is particularly important for the regrowth of neurites after injury. Neurites relay messages to and from the brain to control muscle movement and detect sensations.

In addition to their role in cell movement, microtubules also function as a track along which other proteins, called motor proteins, transport materials within cells. β-tubulin produced from the *TUBB3* gene appears to be important in the attachment of motor proteins to microtubules.

Health Conditions Related to Genetic Changes

Congenital fibrosis of the extraocular muscles

More than 10 mutations in the *TUBB3* gene can cause congenital fibrosis of the extraocular muscles (CFEOM). These mutations most commonly cause a form of the condition called CFEOM3, and they are a rare cause of another form called CFEOM1. Individuals with any form of CFEOM are unable to move their eyes normally; they have difficulty looking upward or, less commonly, side-to-side, and most also have droopy eyelids (ptosis). In addition, people with CFEOM3 can have intellectual disability; behavioral, social, or language problems; or other neurological problems.

The *TUBB3* gene mutations that cause CFEOM change single protein building blocks (amino acids) in the β-tubulin protein. The altered proteins assemble into microtubules, although some do so more readily than others. Research shows that when more altered β-tubulin protein is incorporated into microtubules, the signs and symptoms of the condition are more severe.

Microtubules made with altered β-tubulin proteins do not grow and shrink as they should, which prevents neurite growth. Nerves in the head and face (cranial nerves) that control muscles that surround the eyes (extraocular muscles) are particularly affected, although other nerves can also be involved. Abnormal growth of cranial nerves impairs the function of extraocular muscles, leading to the characteristic features of CFEOM such as restricted eye movement and droopy eyelids. Researchers suspect that abnormal growth of neurites within the brain leads to brain abnormalities that underlie intellectual disability and other neurological problems in some people with CFEOM3.

Certain mutations in the *TUBB3* gene also appear to prevent motor proteins from attaching to microtubules. These mutations typically cause severe CFEOM3 that is associated with additional neurological problems, such as pain, weakness, or a decreased ability to feel sensations in the limbs (peripheral neuropathy) that begins in childhood or adulthood. It is unclear how these genetic changes contribute to specific signs and symptoms in severely affected individuals.

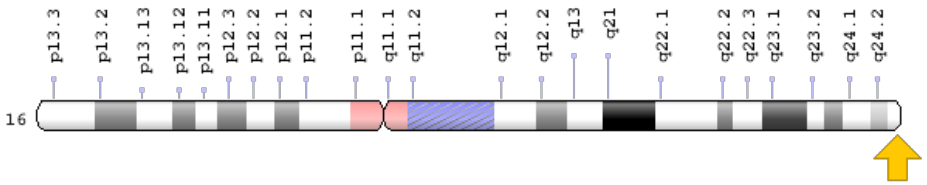
Other disorders

Mutations in the *TUBB3* gene can also cause a condition called cortical dysplasia, complex, with other brain malformations 1 (CDCBM1). The brain abnormalities associated with this condition lead to intellectual disability, weak muscle tone (hypotonia), and progressive muscle stiffness (spasticity) in affected individuals. Brain malformations in CDCBM1 result from abnormal development of the surface of the brain (the cortex) and other regions such as a group of structures deep in the brain called the basal ganglia, which helps control movement; the tissue that connects the left and right halves of the brain (the corpus callosum); and the brainstem, which connects the upper parts of the brain with the spinal cord and regulates many basic body functions. Affected individuals do not typically have problems with the extraocular muscles as in CFEOM (described above). It is thought that mutations in the *TUBB3* gene disrupt the movement of neurons and axons to their correct locations, altering brain development and leading to brain malformations.

Chromosomal Location

Cytogenetic Location: 16q24.3, which is the long (q) arm of chromosome 16 at position 24.3

Molecular Location: base pairs 89,921,925 to 89,936,097 on chromosome 16 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- class III beta-tubulin
- TUBULIN, BETA-3
- Tubulin, Beta 3 Class III Gene
- TUBULIN, BETA, CLASS III

Additional Information & Resources

Educational Resources

- Neuroscience (second edition, 2001): The Actions and Innervation of Extraocular Muscles
  https://www.ncbi.nlm.nih.gov/books/NBK10793/
- The Cell: A Molecular Approach (second edition, 2000): Microtubules
  https://www.ncbi.nlm.nih.gov/books/NBK9932/

Clinical Information from GeneReviews

- Congenital Fibrosis of the Extraocular Muscles
  https://www.ncbi.nlm.nih.gov/books/NBK1348
- Tubulinopathies Overview
  https://www.ncbi.nlm.nih.gov/books/NBK350554

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TUBB3%5BTIAB%5D%29+OR+%28tubulin+beta+3+class+III%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- CORTICAL DYSPLASIA, COMPLEX, WITH OTHER BRAIN MALFORMATIONS 1
  http://omim.org/entry/614039
- TUBULIN, BETA-3
  http://omim.org/entry/602661

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_TUBB3.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TUBB3%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:20772
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:10381
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/10381
- UniProt
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